

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE*In re* Application of:Isaiah J. FIDLER *et al.*

Serial No.: 09/872,162

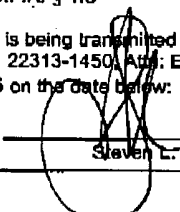
Filed: May 31, 2001

For: ADJUVANT PREPARATION FOR THE
INDUCTION OF SPECIFIC IMMUNITY

Group Art Unit: 1636

Examiner: Q. Nguyen

Atty. Dkt. No.: UTSC:643US/SLH

CERTIFICATE OF FACSIMILE TRANSMISSION 37 C.F.R. § 1.8	
I hereby certify that this correspondence is being transmitted to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, Atty: Examiner Q. Nguyen, GAU 1636, facsimile number 703-872-9306 on the date below:	
May 19, 2004 Date	 Steven L. Highlander

DECLARATION OF DR. PATRICK HWU UNDER 37 C.F.R. §1.132Commissioner for Patents
PO Box 1450
Alexandria, VA 22313-1450


I, the undersigned, do declare that:

1. I am a citizen of United States of America residing in Houston, Texas. I currently hold the position of Professor and Chairman, Department of Melanoma Medical Oncology at M.D. Anderson Cancer Center, Houston, TX.
2. I have over 14 years of experience in laboratory and clinical research in the field of cancer immunotherapy. A copy of my *curriculum vitae* is attached.

3. I have reviewed the content of U.S. Serial No. 09/872,162 ("the '162 application"), and I am familiar with the experimental results described therein.
4. I find the results reported in the '162 application to be quite striking. The inventors have found that injection of the insect cell preparation of the invention not only induces the regression of primary cancer lesions, but more importantly, distant brain metastases as well. The regression of distant metastases is both surprising and significant in that it implies induction of system immunity. This is confirmed by the fact that the treatment effect is reduced in the absence of CD4 or CD8 T-cells. These findings are clinically relevant, since cancer patients normally die of disseminated metastatic disease. Overall, the results of this work could not have been predicted by any prior reports in the literature of which I am aware.
5. I hereby declare that all statements made herein of my knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States Code and that such willful false statements may jeopardize the validity of the application or any patent issued thereon.

5-7-04

Date



Patrick Hwu, MD

THE UNIVERSITY OF TEXAS
MD ANDERSON
CANCER CENTER

Patrick Hwu, M.D.

PRESENT TITLE AND AFFILIATION

Professor of Medicine
Chairman, Department of Melanoma Medical Oncology
The University of Texas M. D. Anderson Cancer Center
Houston, Texas 77030

CITIZENSHIP AND VISA STATUS (if appropriate)

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HOME ADDRESS

3024 Rice Blvd.
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1515 Holcombe Boulevard, Box 430
Houston, TX 77030

EDUCATION

- 1983-1987 The Medical College of Pennsylvania (MCP)
M.D., Class of '87
Magna Cum Laude
- 1981-1983 Lehigh University
B.A. in Premedical Science, as part of Lehigh/MCP six-year BA/MD
program.
Cumulative Grade Point Average: 4.0
Summa Cum Laude

CREDENTIALS

Board Certification

American Board of Internal Medicine
American Board of Medical Oncology

EXPERIENCE/SERVICE

Academic Appointments

- 1993-2003 Senior Investigator, The National Cancer Institute, Bethesda, MD.
- 1989-1993 Clinical Associate, Medical Oncology and Immunotherapy
The National Cancer Institute, Bethesda, MD.

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1987-1989 House officer in the Department of Internal Medicine, The Johns Hopkins Hospital, Department of Internal Medicine, Baltimore, MD.

Academic Administrative Appointments/Responsibilities

Associate Director, Center for Cancer Immunology Research, M.D. Anderson Cancer Center.

Institutional Committee Activities

1999-2003 Co-Chair, NCI Animal Care and Use Subcommittee

Other Appointments/Responsibilities

N/A

Consultantships

N/A

Military or Other Governmental Service

N/A

HONORS AND AWARDS

2002	NCI Center for Cancer Research Federal Technology Transfer Award
2002	Performance Award, NCI Surgery Branch
2000	Exceptional Pay Increase, NCI Surgery Branch
1998	Performance Award, NCI Surgery Branch
1997	Intramural Research Award, Division of Clinical Science, NCI
1992	American Society of Clinical Oncology Travel Award
1987	Dept. of Medicine Prize for academic and clinical excellence (MCP)
1987	Dean's Prize for a high level of accomplishment and outstanding potential (MCP)
1986	Alpha Omega Alpha Medical Honor Society
1986	AOA award for most outstanding work of the sophomore year (MCP)
1985	AOA National Student Research Fellowship
1985	Freshman Anatomy Award in Gross Anatomy, Microanatomy, and Neuroanatomy
1983	Phi Beta Kappa Honor Society
1983	Alumni Association Junior Prize for highest GPA in junior class (Lehigh University)
1982	Wilbur Prize for highest GPA in sophomore class (Lehigh University)
1982	Phi Eta Sigma National Honor Society (Lehigh University)
1981	National Youth Science Camp
1981	National Presidential Scholar
1981	National Merit Scholar

Awards received by members of the Hwu Lab

- Thomas Daly, HHMI Research Scholars Program
1993 HHMI Medical School Fellowship Support Program Award
Project: Redirection of lymphocytes against a colon cancer antigen using a chimeric antibody/T-cell receptor gene
- Mark Reeves, M.D., Ph.D.
1996 NIH Fellows Award for Research Excellence
Project: Transduction and differentiation of dendritic cells from human hematopoietic progenitor cells
- Gang Wang, Ph.D.
1997 NIH Fellows Award for Research Excellence
Project: In vivo redirection of immune cells against tumor using murine hematopoietic stem cells retrovirally transduced with a chimeric monoclonal antibody/T-cell receptor gene
- Richard Royal, M.D.
1997 ASCO (American Society of Clinical Oncology) Travel Award
Project: Dendritic cells transduced with the gene encoding GP100 generate specific anti-melanoma T-cells
- Jennifer Specht, HHMI Research Scholars Program
1997 HHMI Medical School Fellowship Support Program Award
Project: Dendritic cells retrovirally transduced with a model antigen gene are therapeutically effective against established pulmonary metastases
- Michael Kershaw, Ph.D.
1999 NIH Fellows Award for Research Excellence
Project: The generation of gene modified T cells reactive against the angiogenic receptor KDR found on tumor vasculature
- Mark John Sloan, HHMI Research Scholars Program
2000 Farr Scholar, Yale University
Project: Dendritic cells transduced with antigen genes stimulate both CD4+ and CD8+ T-cells
- Rejean Lapointe, Ph.D.
2000 NIH Fellows Award for Research Excellence
Project: A novel method to generate tumor-reactive T-cells using CD40 activated B-cells pulsed with cell lysates
- Russell Pachynski, HHMI Research Scholars Program
2002 Minority Trainee Research Forum Award
Project: Transduction of T-cells with CXCR-2 to enhance migration to chemokines produced by tumors

-Russell Pachynski, HHMI Research Scholars Program
2002 HHMI Medical School Fellowship Support Program Award
Project: Transduction of T-cells with CXCR-2 to enhance migration to chemokines

RESEARCH

Grants and Contracts

None

Funded Protocols/NIH Intramural Program (until September 1, 2003)

Principle Investigator for the following clinical protocols:

Immunization with Dendritic Cells Presenting Epitopes Derived from the Melanoma Associated Antigens Mart-1 and gp100 in Patients with Metastatic Melanoma

Treatment of Patients with Advanced Epithelial Ovarian Cancer using Peripheral Blood Lymphocytes Transduced with a Gene Encoding a Chimeric T-Cell Receptor Reactive with Folate Binding Protein

A Phase II Protocol of Flt3 Ligand in Patients with Metastatic Melanoma and Renal Cancer (closed)

Treatment of Patients with Metastatic Melanoma and Renal Cancer with a Combination of Flt3L and CD40L (closed)

Associate Investigator for the following clinical protocols (until September 1, 2003):

Treatment of Patients with Metastatic Melanoma Using Cloned Lymphocytes Following the Administration of a Nonmyeloablative but Lymphocyte Depleting Regimen

An open-label study of MDX-CTLA4 in combination with gp100 peptides emulsified with Montanide ISA 51 in the treatment of patients with stage IV melanoma

Immunization of Patients with Metastatic Melanoma Using Recombinant Fowlpox Virus Encoding a gp100 Peptide Preceded by an Endoplasmic Reticulum Insertion Signal Sequence

Immunization of HLA-A*0201 Patients with Metastatic Cancer Using a Modified Epitope from the ESO-1 Antigen

Immunization of HLA-A*0201 Patients with Metastatic Cancer Using a Peptide Epitope from the Telomerase Antigen

Immunization of HLA-A0201 positive patients with metastatic melanoma using a peptide from tyrosinase-related protein 2 (TRP-2)

Immunization of Patients with Metastatic Melanoma Using a Class II Restricted Peptide from the GP100 Antigen and Class I Restricted Peptides from the GP100 and MART-1 Antigens

Immunization of Patients with Metastatic Melanoma Using MART-1 and GP100 Peptides Modified to Increase Binding to HLA-0201
Randomized Comparison of Three Schedules of Peptide Immunization in Patients at High Risk for Recurrence of Melanoma

Treatment of Patients with Metastatic Melanoma Using Cloned Peripheral Blood Lymphocytes Sensitized In Vitro to the gp209-2M Immunodominant Peptide

A Phase I Trial of a Live, Genetically Modified Salmonella Typhimurium (VNP20009) for the Treatment of Cancer by Intravenous Administration (closed)

Immunization of Patients with Metastatic Melanoma Using the GP100 Peptide Preceded by an Endoplasmic Reticulum Insertion Signal Sequence (closed)

Immunization of Patients with Metastatic Melanoma Using DNA Encoding the GP100 Melanoma

Immunization of Patients with Metastatic Melanoma Using Immunodominant Peptides from the Tyrosinase Protein, Tyrosinase Related Protein-1 (TRP1), or GP100 Protein (closed)

Phase I Trial in Patients with Metastatic Melanoma of Immunization with a Recombinant Fowlpox Virus Encoding the gp100 Melanoma Antigen (closed)

Immunization of Patients with Metastatic Melanoma Using Recombinant Fowlpox and Vaccinia Viruses Encoding the Tyrosinase Antigen (closed)

Treatment of Patients with Metastatic Renal Cell Carcinoma with Neutralizing Antibody to Vascular Endothelial Growth Factor (VEGF); (closed)

A Randomized Three-Arm Study of the Treatment of Patients with Metastatic Renal Cell Carcinoma Using Low-Dose IL-2 versus High-Dose IL-2 (closed)

Patents Granted and Pending

Patents Pending:

Methods and compositions for transforming dendritic cells and activating T cells (U.S. Patent Application No. 09/117,764)

Chimeric receptor genes and cells transformed therewith (U.S. Patent Application 08/547,263)

Activated Dual Specificity Lymphocytes and their Methods of Use

(US Patent Application No. 09/803,578)

A novel class II restricted epitope from the melanoma antigen gp100
(U.S. provisional patent application 60/314,183)

Methods for treating cancer in humans using IL-21
(U.S. Provisional Patent Application Serial No. 60/368,438)

Grant Reviewer/Service on NIH/Other Study Sections

2003 Department of Defense (DOD) Ovarian Cancer Study Section

PUBLICATIONS

a. Articles in Peer-Reviewed JournalsPublications

1. Young H, L Varesio, and Hwu P Post-Transcriptional Control of Human Interferon-Gamma Gene Expression in Transfected Mouse Fibroblasts. *Molecular and Cellular Biology*. 6(6): 2253-2256, 1986.
2. Dempsey WL, Hwu P, D Russell, and Morahan PS. Bone Marrow Derived Macrophages have Polyamine and Ectoenzyme Phenotypes Distinct from Resident Macrophages. *Life Sciences*. 42(20): 2019-27, 1988.
3. Karp S, Hwu P, A Farber, N Restifo, M Kriegler, J Mulé, and SA Rosenberg. In vivo Activity of TNF Mutants: Secretory But Not Membrane Bound TNF Mediates the Regression of Retrovirally Transduced Murine Tumor. *Journal of Immunology*. 149: 2076-2081, 1992.
4. Hwu P, S Schwarz, M Custer, C Smith, J Mule, and SA Rosenberg. Detection of TNF Secretion in Cultures of Tumor Infiltrating Lymphocytes Using Soluble TNF Receptor. *Journal of Immunological Methods*. 151: 139-147, 1992.
5. Yannelli J, C Hyatt, S Johnson, SA Rosenberg. Characterization of Human Tumor Cell Lines Transduced with Hwu, P., the cDNA Encoding Either Tumor Necrosis Factor α or Interleukin-2. *Journal of Immunological Methods* 161: 77-90, 1993.
6. Karp S, A Farber, J Salo, Hwu P, G Jaffe, A Asher, N Restifo, J Mulé, and SA Rosenberg. Cytokine Secretion by Genetically Modified Nonimmunogenic Murine Fibrosarcoma: Tumor Inhibition by IL2 But Not TNF. *Journal of Immunology*. 150: 896-908, 1993.
7. Rosenberg SA, WF Anderson, M Blaese, Hwu P, J Yannelli, J Yang, S Topalian, D Schwartzentruber, J Weber, S Ettinghausen, D Parkinson, and D White. The Development of Gene Therapy for the Treatment of Cancer. *Annals of Surgery* 218: 455-464, 1993.

8. Hwu P, J Yannelli, M Kriegler, WF Anderson, C Perez, Y Chiang, S Schwarz, R Cowherd, C Delgado, J Mulé, and SA Rosenberg. Functional and Molecular Characterization of TIL Transduced with the TNF α cDNA for the Gene Therapy of Cancer in Man. *Journal of Immunology* 150: 4104-4115, 1993.
9. Hwu P, G Shafer, J Treisman, D Schindler, G Gross, R Cowherd, SA Rosenberg, Z Eshhar. Lysis of Ovarian Cancer Cells by Human Lymphocytes Redirected with a Chimeric Gene Composed of an Antibody Variable Region and the Fc Receptor γ Chain. *J. of Experimental Medicine* 178: 361-366, 1993.
10. Treisman J, Hwu P, J Yannelli, G Shafer, R Cowherd, D Samid, SA Rosenberg. Upregulation of Tumor Necrosis Factor Alpha Production by Retrovirally Transduced Human Tumor Infiltrating Lymphocytes using Trans-Retinoic Acid. *Cellular Immunology* 156: 448-457, 1994.
11. Hwu P and SA Rosenberg. 1994. The Genetic Modification of T Cells for Cancer Therapy: An Overview of Laboratory and Clinical Trials. *Cancer Detection and Prevention* 18(1): 43.
12. Hwu P What the Future Holds for Gene Therapy. *Internal Medicine* 15(2): 39, 1994.
13. Hwu P and SA Rosenberg. The Use of Gene Modified TIL for Cancer Therapy. *Annals of the NYAS* 716: 188-199, 1994.
14. Treisman J, Hwu P, S Minamoto, G Shafer, R Cowherd, R Morgan, and SA Rosenberg. Interleukin-2-transduced lymphocytes grow in an autocrine fashion and remain responsive to antigen. *Blood* 85:139-145, 1995.
15. Hwu P, JC Yang, R Cowherd, J Treisman, Z Eshhar, and SA Rosenberg. In vivo efficacy of T-cells redirected with chimeric antibody/T-cell receptor genes. *Cancer Research*. 55: 3369-3373, 1995.
16. Royal R, Steinberg S, White D, Hwu P, Marincola F, Parkinson D, Schwartzentruber D, Topalian S, Yang J, and SA Rosenberg. Correlates of response to IL-2 therapy in patients treated for metastatic renal cancer and melanoma. *The Cancer Journal from Scientific American* 2(2): 91-98, 1996.
17. Chamberlain R, Carroll M, Bronte V, Hwu P, Warren S, Yang J, Nishimura M, Moss B, Rosenberg SA, and N Restifo. Costimulation enhances the active immunotherapy effect of model recombinant anti-cancer vaccines. *Cancer Research* 56:2832-2836, 1996.
18. Lam J, Reeves M, Cowherd R, Rosenberg SA, and Hwu P. Gene transfer into lymphocytes is improved with retroviral vectors utilizing the gibbon ape leukemia virus envelope. *Human Gene Therapy* 7:1415-1422, 1996.

19. Reeves ME, Lam JS, R Royal, Rosenberg SA, and Hwu P. Retroviral transduction of human dendritic cells with a tumor-associated antigen gene. *Cancer Research* 56:5672-5677, 1996.
20. Hwu P. Current challenges in cancer gene therapy. *Journal of Internal Medicine*. 242 (supplement 740): 109-114, 1997.
21. Pack S, Karkera J, Zhuang Z, Pak E, Hwu P, Balan K, Park WS, Pham T, Ault D, Moshe G, Liotta L, Detera-Wadleigh S, Wadleigh R. Molecular cytogenetic fingerprinting of esophageal squamous cell carcinoma using comparative genomic hybridization reveals consistent pattern of chromosomal alterations. *Genes Chromosomes Cancer* 25:160-168, 1998.
22. Wu P, Alexander HR, Huang J, Hwu P, Gnant M, Berger A, Turner E, Wilson O, and SK Libutti. In vivo sensitivity of human tumors to tumor necrosis factor- α is determined by tumor production of the novel cytokine endothelial-monocyte activating polypeptide II. *Cancer Research*. Jan 1;59(1):205-12, 1999.
23. Rosenberg SA, Yang JC, Schwartzentruber DJ, Hwu P, Marincola FM, Topalian SL, Restifo N, Dudley ME, Schwarz SL, Spiess PJ, Wunderlich JR, Parkhurst MR, Kawakami Y, Seipp CA, Einhorn JH, and White DE. Immunologic and therapeutic evaluation of a synthetic peptide vaccine for the treatment of patients with metastatic melanoma. *Nature Medicine* 4(3): 321-327, 1998.
24. Specht JM, Wang G, Do M, Lam JS, Royal R, Reeves M, Rosenberg SA, and Hwu P. Dendritic cells retrovirally transduced with a model antigen gene are therapeutically effective against established pulmonary metastases. *J. Exp. Med.* 186(8): 1213-1221, 1997.
25. Wang G, Chopra R, Royal R, Yang J, Rosenberg SA, and Hwu P. A T-cell independent anti-tumor response in mice using bone marrow cells retrovirally transduced with a chimeric monoclonal antibody/Fc- γ receptor gene recognizing a human ovarian cancer antigen. *Nature Medicine* 4 (2):168-172, 1998.
26. Rosenberg SA, Zhai Y, Yang JC, Schwartzentruber DJ, Hwu P, Marincola FM, Topalian SL, Restifo NP, Seipp CA, Einhorn JH, Roberts B, White. 1998. Immunizing patients with metastatic melanoma using recombinant adenoviruses encoding MART-1 or gp100 melanoma antigens. *J Natl Cancer Inst* Dec 16;90(24):1894-900, 1998.
27. Rosenberg SA, Yang JC, Schwartzentruber DJ, Hwu P, Marincola FM, Topalian SL, Seipp CA, Einhorn JH, White DE, Steinberg SM. Prospective randomized trial of the treatment of patients with metastatic melanoma using chemotherapy with cisplatin, dacarbazine, and tamoxifen alone or in combination with interleukin-2 and interferon alfa-2b. *J Clin Oncol* Mar;17(3):968-75, 1999.

28. Bronte V, Chappell D, Apolloni E, Cabrelle A, Wang M, Hwu P, and N Restifo. Tumors that secrete GM-CSF inhibit CD8+ T cell responses by dysregulating antigen presenting cell maturation. *Journal of Immunology* May 15;162(10):5728-37, 1999.
29. Moir S, Lapointe R, Malaspina A, Ostrowski M, Cole C, Chun T, Adelsberger J, Baseler M, Hwu P, and A Fauci. CD40-mediated induction of CD4 and CXCR4 on B-lymphocytes correlates with restricted susceptibility to human immunodeficiency virus type 1 infection: potential role of B-lymphocytes as a viral reservoir. *Journal of Virology* 73(10):7972-80, 1999.
30. Clay T, Custer M, Sachs J, Hwu P, Rosenberg, S., and M. Nishimura. Efficient transfer of a tumor antigen-reactive TCR to human peripheral blood lymphocytes confers anti-tumor reactivity. *Journal of Immunology* 163(1):507-13, 1999.
31. Rosenberg SA, Yang JC, Schwartzentruber DJ, Hwu P, Marincola FM, Topalian SL, Restifo NP, Sznol M, Schwarz SL, Spiess PJ, Wunderlich JR, Seipp CA, Einhorn JH, Rogers-Freezer L, White DE. Impact of cytokine administration on the generation of antitumor reactivity in patients with metastatic melanoma receiving a peptide vaccine. *J Immunology* 163(3):1690-5, 1999.
32. Feldman A, Restifo N, Alexander HR, Bartlett D, Hwu P, Seth P, and Libutti S. Antiangiogenic gene therapy of cancer utilizing a recombinant adenovirus to elevate systemic endostatin levels in mice. *Cancer Research* 60(6):1503-6, 2000.
33. Daly T, Royal R, Kershaw M, Treisman J, Wang G, Li W, Herlyn D, Eshhar Z, and Hwu P. Recognition of human colon cancer by T cells transduced with a chimeric receptor gene. *Cancer Gene Therapy* 7(2):284-91, 2000.
34. Chinnasamy N, Chinnasamy D, Toso J, Lapointe R, Candotti F, Morgan R and Hwu P. Efficient Gene Transfer To Human Peripheral Blood Monocyte Derived Dendritic Cells Using HIV-1 Based Lentiviral Vectors *Human Gene Therapy* Sep 1;11(13):1901-9, 2000.
35. Kershaw M, Westwood J, Zhu Z, Witte L, Libutti S and Hwu P. 2000 The generation of gene modified T cells reactive against the angiogenic receptor KDR found on tumor vasculature. *Human Gene Therapy* Dec 10;11(18):2445-52, 2000.
36. Hwu P, Du M X, Lapointe R, Do M, Taylor M W, Young H A. IDO production by human dendritic cells results in the inhibition of T-cell proliferation *J. of Immunology* 164: 3596-3599, 2000.
37. Parker L L, Do M T, Westwood J A, Wunderlich J R, Dudley M E, Rosenberg SA, and Hwu P. Expansion and Characterization of T cells Transduced with a Chimeric Receptor against Ovarian Cancer *Human Gene Therapy* Nov 20;11(17):2377-87, 2000.

38. Lapointe R, Toso J F, Butts C, Young H A, and Hwu P. Human dendritic cells require multiple activation signals for the efficient generation of tumor antigen-specific T lymphocytes. *European Journal of Immunology* Nov;30(11):3291-8, 2000.
39. Moir Susan, Angela Malaspina, Kisani Ogwaro, Eileen T Donoghue, Claire W Hallahan, Linda A Ehler, Shuying Liu, Joseph Adelsberger, Réjean Lapointe, **Hwu P**, Michael Baseler, Jan M Orenstein, Tae-Wook Chun, Jo Ann M Mican and Antony S Fauci. HIV-1 induces phenotypic and functional perturbations of B cells in chronically infected individuals. *Proc Natl Acad Sci U S A*; Aug 28;98(18):10362-10367, 2001.
40. Toso J F, Gill V, Witebsky F, **Hwu P**, Maríncola F, Restifo N, Schwartzentruber D, Sherry R, Topalian S, Yang J, Freezer L, Morton K, Seipp C, Haworth L, Mavroukakis S, White D, Sznol M, and SA Rosenberg. Phase I study of the intravenous administration of attenuated *Salmonella typhimurium* to patients with metastatic melanoma. *J. Clinical Oncology* Jan 1;20(1):142-52, 2002.
41. Dudley ME, Wunderlich J, Nishimura M, Yu D, Yang J, Topalian S, Schwartzentruber D, **Hwu P**, Maríncola F, Sherry R, Leitman S, and S A Rosenberg. Adoptive transfer of cloned, melanoma-reactive T lymphocytes for the treatment of patients with metastatic melanoma. *J Immunother* 2001 Jul-Aug;24(4):363-73, 2001.
42. Dudley M, Wunderlich J, Yang J, **Hwu P**, Schwartzentruber D, Topalian S, Sherry R, Maríncola F, Leitman S, Seipp C, Rogers-Freezer L, Morton K, Mavroukakis S, White D, and S A Rosenberg. A phase I study of non-myeloablative chemotherapy and adoptive transfer of autologous tumor antigen-specific T lymphocytes in patients with metastatic melanoma. *J. of Immunotherapy* May-Jun;25(3):243-51, 2001.
43. **Hwu P** and Freedman R. The Immunotherapy of Ovarian Cancer. *J. of Immunotherapy* May-Jun;25(3):189-201, 2002.
44. Royal R E, Reeves ME, Wang G, Daly T, Treisman J, Lam J, Kershaw M H, **Hwu P**. Increased Chimeric T-cell Receptor Functional Expression in Human PBL Using Retroviral Vectors Modified with IRES and Splicing Motifs. *Gene Therapy*. Aug;9(16):1085-92, 2002.
45. Marroquin C E, Westwood J A, Lapointe R, Mixon A, Wunderlich J R, Caron D, Rosenberg S A, **Hwu P**. Mobilization of DC precursors in cancer patients by Flt3L allows the generation of higher yields of cultured DCs. *J. of Immunotherapy* May-Jun;25(3):278-88, 2001.
46. Dudley M E, Wunderlich J R, Yang J C, **Hwu P**, Schwartzentruber D J, Topalian S L, Sherry R M, Maríncola F M, Leitman S F, Seipp C A, Rogers-Freezer L, Morton K E, Nahvi A, Mavroukakis S A, White D E, Rosenberg S A. A phase I study of nonmyeloablative chemotherapy and adoptive transfer of autologous tumor antigen-specific T lymphocytes in patients with metastatic melanoma. *J Immunother*. 2002 May-Jun;25(3):243-51.

47. Wang H Y, Fu T, Wang G, Zeng G, Perry-Lalley D M, Yang J C, Restifo N P, **Hwu P**, Wang R F. Induction of CD4(+) T cell-dependent antitumor immunity by TAT-mediated tumor antigen delivery into dendritic cells. *J Clin Invest*. 2002 Jun;109(11):1463-70.
48. Royal R E, Kershaw M H, Reeves M E, Wang G, Daly T, Treisman J, Lam J, **Hwu P**. Increased functional expression of transgene in primary human lymphocytes using retroviral vectors modified with IRES and splicing motifs. *Gene Ther*. 2002 Aug;9(16):1085-92.
49. Touloukian C E, Leitner W W, Robbins P F, Li Y F, Kang X, Lapointe R, **Hwu P**, Rosenberg S A, Restifo N P. Expression of a "self"-antigen by human tumor cells enhances tumor antigen-specific CD4(+) T-cell function. *Cancer Research*. Sep 15;62(18):5144-7, 2002.
50. Sloan J M, Kershaw M H, Touloukian C, Lapointe R, Robbins P, Restifo N P, and **Hwu P**. MHC Class I and Class II Presentation of Tumor Antigen in Retrovirally and Adenovirally Transduced Dendritic Cells. *Cancer Gene Therapy*. Nov;9(11):946-50, 2002.
51. Toso J F, Lapointe R, Rosenberg S A and **Hwu P**. CD40 Ligand and Lipopolysaccharide Enhance the *In Vitro* Generation of Melanoma-Reactive T-cells. *J. Imm. Methods*. 259(1-2):181-90, 2002.
52. Kershaw M H, Hsu C, Mondesire W, Parker L L, Wang G, Overwijk WW, Lapointe R, Yang J C, Wang R, Restifo N P, and **Hwu P**. Immunization against endogenous retroviral tumor associated antigens. *Cancer Research*. 61(21):7920-4, 2001.
53. Lapointe R, Royal R, Reeves M, Robbins P, and **Hwu P**. Identification of a novel class II restricted epitope from gp100 using retrovirally transduced dendritic cells. *J. of Immunology* 167: 4758-4764, 2001.
54. Kershaw M H, Wang G, Westwood J A, Pachynski R K, Tiffany H L, Wang E, Marincola F M, Tiffany L, Young H A, Murphy P M, and **Hwu P**. Redirecting migration of T-cells to chemokine secreted from tumors by genetic modification with CXCR2. *Human Gene Therapy* Nov;13(16):1971-80, 2002.
55. Wang H Y, Fu T, Wang G, Zeng G, Perry-Lalley D M, Yang J C, Restifo N P, **Hwu P**, and Wang R F. TAT-mediated tumor antigen delivery into dendritic cells for generation of potent antitumor immunity. *Journal of Clinical Investigation* Jun;109(11):1463-70, 2002.
56. Dudley M E, Wunderlich J, Robbins P, Yang J C, **Hwu P**, Schwartzentruber D J, Topalian S L, Sherry R, Restifo N, Hubicki A M, Robinson M R, Raffeld M, Duray P, Seipp C A, Rogers-Freezer L, Morton K E, Mavroukakis S A, White D E, Rosenberg S A. Cancer regression and autoimmunity following clonal

repopulation with anti-tumor lymphocytes and non-myeloablative conditioning. *Science* 25;298(5594):850-4, Oct, 2002.

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58. O'Reilley F, Feldman E, Yang J, Hwu P, Turner ML. Recurring cutaneous eruption in a patient with metastatic renal cell carcinoma being treated with high-dose interleukin 2. *J Am Acad Dermatol* 48(4):02-4, April, 2003.
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60. Lapointe R, Bellemare-Pelletier A, Housseau F, Thibodeau J, Hwu P. D40-stimulated B lymphocytes pulsed with tumor antigens are effective antigen presenting cells that can generate specific T cells *Cancer Res* 63(11):2836-43, June, 2003.
61. Phan G Q, Yang J C, Sherry R M, Hwu P, Topalian S L, Schwartzentruber DJ, Restifo N P, Haworth L R, Seipp C A, Freezer L J, Morton KE, Mavroukakis S A, Duray PH, Stenberg SM, Allison JP, Davis TA, Rosenberg S A. Cancer regression and autoimmunity induced by cytotoxic T lymphocyte-associated antigen 4 blockade in patients with metastatic melanoma. *Proc Natl Acad Sci* 100(14):8372-8377, July, 2003.
62. Phan G Q, Touloukian C E, Yang J C, Restifo N P, Sherry RM, Hwu P, Topalian S L, Schwartzentruber D J, Seipp C A, Freezer L J, Morton K E, Mavroukakis S A, White D E, Rosenberg S A. Immunization of patients with metastatic melanoma using both class I- and class II-restricted peptides from melanoma-associated antigens. *Cancer Research. J Immunother.* 2003 Jul-Aug;26(4):349-56.
63. Yang J C, Haworth L, Sherry R M, Hwu P, Schwartzentruber D J, Topalian S L, Steinberg S M, Chen H, and Rosenberg S A. A randomized double-blind placebo-controlled trial of bevacizumab (anti-VEGF antibody) demonstrating a delay in tumor progression in patients with metastatic renal cancer. *New England Journal of Medicine.* 2003 Jul 31;349(5):427-34.
64. Yang J C, Sherry R M, Steinberg S M, Topalian S L, Schwartzentruber D J, Hwu P, Seipp C A, Rogers-Freezer L, Morton K E, White D E, Liewehr D, Merino M, and S A Rosenberg. A randomized comparison of high and low-dose interleukin-2 therapies in the treatment of patients with metastatic renal cell carcinoma, *J Clin Oncol*, 21(16): 3127-32, August 15, 2003.

65. Rosenberg S A, Yang J C, Schwartzentruber D J, Hwu P, Topalian S L, Sherry R M, Restifo N P, Wunderlich J R, Seipp C A, Rogers-Freezer L, Morton K E, Mavroukakis S A, Gritz L, Panicali D L, White D E. Recombinant fowlpox viruses encoding the anchor-modified gp 100 melanoma antigen can generate antitumor immune responses in patients with metastatic melanoma. *Clin Cancer Res.* 1;9(8): 2973-80, August, 2003.
66. Rosenberg S A, Yang J C, Robbins P F, Wunderlich J R, Hwu P, Sherry R M, Schwartzentruber D J, Topalian S L, Restifo N P, Filie A, Chang R, Dudley M E. Cell transfer therapy for cancer: lessons from sequential treatments of a patient with metastatic melanoma. *J Immunother.* 2003 Sep-Oct;26(5):385-93.

In Press

Wang G, Tsoi M, Spolski R, Lou Y, Ozaki K, Feng C, Kim G, Leonard W J, Hwu P. In vivo antitumor activity of interleukin 21 mediated by natural killer cells. *Cancer Research.* (in press) Dec. 15, 2003.

Submitted Manuscripts

Rosenberg S A, Yang J, Schwartzentruber D, Hwu P, Marincola F, Topalian S, Sherry R, Restifo N, Seipp C, Freezer L, Morton K, Mavroukakis S, White D, Steinberg S. Immunologic and clinical studies of patients with metastatic melanoma administered immunodominant peptides from melanoma-melanocyte differentiation antigens.

b. Invited Articles

Hwu P. The Gene Therapy of Cancer. *Principles and Practice of Oncology Update Series*, Philadelphia, J.B. Lippincott. 9(4): 1-13-1995.

c. Editorials

N/A

d. Other Articles

N/A

Manuscripts in Preparation

1. Lam JS, Specht J, Royal R E, Reeves M E, Wang G, Restifo NP, and Hwu P. The Ability of Dendritic Cells and Pox Viruses to Treat Established Pulmonary Metastases
2. Hwu P, Rosenberg S A, Treatment of Melanoma Patients with TNF-Transduced TIL.

3. Pachynski RK, Kershaw M, Restifo N, and Hwu P. A comparison of transduction methods for primary murine T-cells
4. Parker L, Kershaw M, Wang G, Lapointe R, Restifo NP, Hwu P. Use of Flt3L as an adjuvant for tumor immunization.

e. Abstracts (Last five years only)
Not Listed

f. Book Chapters

1. Hwu, P. and S.A. Rosenberg. The Genetic Modification of Lymphocytes for Cancer Immunotherapy. Biologic Therapy of Cancer 2nd edition (V. DeVita, S. Hellman, S.A. Rosenberg, ed.) pp.727-737, 1995. Philadelphia: J.B. Lippincott.
2. Hwu, P. and S. Rosenberg. The Gene Therapy of Cancer. Cancer: Principles and Practice of Oncology, 5th Edition. Philadelphia, J.B. Lippincott. 3005-3022 (Ch.60), 1996.
3. Hwu, P. The Genetic Modification of Lymphocytes for Cancer Immunotherapy. Biologic Therapy of Cancer 3rd edition (V. DeVita, S. Hellman, S.A. Rosenberg, ed.), Philadelphia: J.B. Lippincott; Chapter 20.1: 757-769, 2000.
4. Hwu, P. The Gene Therapy of Cancer. Cancer: Principles and Practice of Oncology, 6th Edition. Philadelphia, J.B. Lippincott Chapter 62, 3161-3180, 2001.

g. Books (edited and written)
N/A

h. Letters to the Editor
N/A

i. Manuals, Teaching Aids, Other Publications
N/A

j. Other
N/A

EDITORIAL AND REVIEW ACTIVITIES

Editorial Positions:

Associate Editor, Journal of Immunotherapy

Journal Reviewer

Journal of Immunology, Nature Medicine, Nature Biotechnology, Journal of Experimental Medicine, Cancer Research, Clinical Cancer Research

TEACHING**Within Current Institution****Formal Teaching**

N/A

Courses Taught

N/A

Training Programs

N/A

Other Educational Programs

N/A

Supervisory Teaching

N/A

Advisory Committees

Chemotherapy Errors Reduction Task Force (while at NIH)

Supervisory Committees

N/A

Direct Supervision

N/A

Undergraduate and Allied Health Students

N/A

Medical Students

N/A

Graduate Students

N/A

Residents and Fellows

N/A

Outside of Current Institution**Organization of National or International Conferences/Symposia**

N/A

Presentations at National or International Conferences

Invited Speaker and Lectureship

7th NCI-EORTC Symposium on New Drugs in Cancer Therapy.
Amsterdam, The Netherlands. 1992

U.S.-Israel Workshop on New Treatment Strategies for Cancer, Based on
Molecular Biology. Jerusalem, Israel. 1992

International Symposium on Genetic Factors in Predictive and Preventive
Oncology. Nice, France. 1993

Southwest Oncology Group Spring Meeting: Gene Therapy
Developmental Therapeutics Symposium. Denver, Colorado. 1993

The New York Academy of Sciences conference on Gene Therapy for
Neoplastic Diseases. Washington, D.C. 1993

American Association for Cancer Research Special Conference on
Molecular Approaches to Cancer Immunotherapy. Asheville, North
Carolina. 1993

The Society for Biological Therapy 8th Annual Scientific Meeting.
Nashville, Tennessee. 1993

Weizmann Institute of Science conference on The Immunotherapy and
Gene Therapy of Cancer. Ein Gedi, Israel. 1994

International Symposium on The Impact of Biotechnology on Predictive
Oncology and Therapy. Boston, Mass. 1994

International Symposium of Molecular Cell Biology of Macrophages.
Nagoya, Japan. 1995.

Biotech and Pharm China '95 International Symposium, Shanghai, China
1995

Keystone Symposia on Gene Therapy for Hematopoietic Stem Cells in
Genetic Disease and Cancer. 1996.

Fourth International Congress on Biological Response Modifiers. San
Antonio, Texas. 1997.

XIVth Meeting of the International Society of Hematology. Stockholm,
Sweden. 1997.

Immunotherapy of Ovarian Cancer. Massachusetts General Hospital
Symposium. Boston, MA 1998.

Eric K. Fernstrom Symposium on Gene Therapy of the Haematopoietic
System and the CNS. Lund, Sweden. 1998.

Yale University School of Medicine Gene Therapy Lecture Series. New
Haven, Conn. 1999

American Society of Gene Therapy. Denver, CO 2000

Ludwig Institute for Cancer Research, Lausanne, Switzerland 2001

Eurocancer 2001, Paris, France

Mayo Clinic (Jacksonville), Jacksonville Florida 2002

Cancer Center Grand Rounds, University of Rochester, Rochester, NY
2002

Cleveland Clinic Cancer Center, Cleveland, Ohio 2002

Moffitt Cancer Center Grand Rounds. Tampa, Florida 2002

Society of Biologic Therapy Annual Meeting, San Diego, CA 2002

Development of Therapeutic Cancer Vaccines, Los Angeles, CA 2003

Basic Aspects of Tumor Immunology, Keystone, CO 2003

Other, Including Scientific Exhibitions

N/A

Seminar Invitations from Other Institutions

Listed above under Invited Speaker and Lectureship

Lectureships and Visiting Professorships

N/A

Other Presentations (state, local), Conferences

N/A

PROFESSIONAL MEMBERSHIPS/ACTIVITIES

Professional Society Activities, with Offices Held

None

Local/State

None

National and International

International Society of Biologic Therapy

American Society of Clinical Oncology (ASCO)

American Association for Cancer Research (AACR)

American Association of Immunology (AAI)

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OTHER
None